

REMARKS

After amendment, claims 94-99 remain pending in the present application, claims 1-93 having been cancelled pursuant to the filing of the instant application, the Examiner's issuance of a restriction requirement and Applicant's decision to advance prosecution of this application in seeking allowance of the presently claimed subject matter. Note that the present claims are directed to *pharmaceutical compositions*, not compounds *per se*. Note that the subject matter which has been cancelled from this application is cancelled *without prejudice*, in order to expedite allowance of the instant application. It is anticipated that Applicants will file one or more divisional applications directed to cancelled subject matter. No new matter has been added by way of this amendment.

The Examiner has rejected previously filed claims 94-99 under 35 U.S.C. §103 as being obvious over Petit, et al., *J. Natural Products*, (1984) 47, 913-919 ("Petit") taken with Faber, et al., *Helv. Chim.*, (1993) vol. 56, 2282-2284 ("Faber") for the reasons which are stated in the office action on pages 2-3. Applicants respectfully submit that the claims as amended and presented do not raise issues under 35 U.S.C. §103 and should be considered allowable for the reasons which are stated hereinbelow.

The 35 USC §103 Rejection

The Rejection of Claims 94-99 over Petit, taken with Faber

The Examiner has rejected previously pending claims 94-99 as being unpatentable over Petit, in view of Faber for the reasons which are stated in the office action on page 2-3. In particular, the Examiner argues that Petit teach compounds and methods of use. The Examiner cites Faber for teaching analogous compounds, with differences associated with the position of certain substituents. The Examiner argues that given the similarity of the structures which are disclosed in Petit and Faber, one of ordinary skill in the art would be motivated to make the claimed compositions in searching for compounds exhibiting pharmaceutical activity. The Examiner therefore concludes that the previously filed claims 94-99 are unpatentable as being

obvious over a combination of the disclosure of the cited references. Applicants respectfully traverse the Examiner's rejection and submit that the presently pending claims, which are directed to compositions which comprise compounds which are not suggested by the prior art references, are clearly patentable over those references.

The present invention, which, in its broadest terms is claimed in claims 94-99 is directed to pharmaceutical compositions which comprise effective amounts of compounds as set forth in claims. Applicants have carefully reviewed Petit and Faber and respectfully submit that the presently claimed compositions are patentable over those references. Note that in the present compounds there are at least two substituents (represented by OR₁ and OR₂) which are substituted at distal ends of the phenanthrene groups of the molecule and a substituent at R₅ (in other words, R₅ is not H). Moreover, the hydrogen atom on the bridge carbon at the position alpha to R₅ is set forth as is claimed. Applicants have discovered that the claimed groups are required for activity associated with pharmaceutical compositions and instill enhanced activity for the compounds which are included in the claimed pharmaceutical compositions. Many of the claimed compositions of the present invention include compounds which contain four non-hydrogen substituents in the phenanthrene portion of molecule. Neither of the references which are relied upon by the Examiner set forth the substituents on the phenanthrene portion of the molecule in combination with the configuration for the hydrogen and the inclusion of a substituent at R₅ as claimed in the present invention. Applicants have determined that compounds which contain a hydrogen in the configuration as claimed are far more active (anticancer) than compounds which contain a hydrogen in the same location of the molecule wherein the hydrogen is oriented in a "down" or alpha configuration. It is respectfully submitted that none of the references disclose or suggest pharmaceutical compositions as claimed.

Petit is a deficient reference and fails to disclose or suggest the present compounds or pharmaceutical compositions. Petit does disclose certain compounds as having anti-neoplastic activity, but does not provide any structure activity relationship data associated with other compounds which are disclosed or suggested. One of ordinary skill, relying on Petit would not be lead to the compounds/compositions of the present invention. In particular, compounds 1a and 1b of Petit do not disclose the present invention, and do not provide information sufficiently

useful to provide the present invention. Petit does not disclose the four particular substituents in the two phenyl groups of the compounds used in the present invention, does not suggest the requirement for substituents as claimed at positions R₁ and R₂ (i.e., at distal positions) of the phenanthrene ring, does not disclose that R₅ must be a substituent as claimed (e.g., is not H), does not disclose that the bridge substituent should be a hydrogen as presented in the claims and provides no structure activity relationship from which one of ordinary skill could glean the identification of the substituents which influence activity. In short, there is simply an insufficient disclosure from which one of ordinary skill might find useful information to provide the compositions of the present invention. Petit is clearly a deficient reference in failing to disclose or suggest the present invention.

Turning to Faber, this reference is barely relevant to the present invention. Faber provides stereospecific syntheses of certain compounds which are disclosed therein. The compounds which are disclosed are not those of the present invention. Notwithstanding that clear deficiency, there is absolutely no discussion or suggestion of any biological activity whatsoever in Faber. In short, Faber does absolutely nothing to obviate the deficiencies of Petit in failing to disclose or suggest the present invention.

Under the prevailing caselaw, *KSR International Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), it remains necessary to identify some reason that would have led a person of ordinary skill in the art to modify a known composition in a particular manner to establish *prima facie* obviousness of a new claimed composition.” *Takeda Chem. Indus., Ltd. v. Alphapharm Pty., Ltd.*, 492 F.3d 1350, 1357 (Fed. Cir. 2007). Additionally, there must be a reasonable expectation that the asserted combination would prove successful. *Id.*

Here, there was no motivation to modify and combine Petit and Faber to yield the claimed invention in the manner suggested by the Examiner, nor did skilled artisans have any reason to believe that the combination of Petit and Faber as suggested by the Examiner would prove successful. This is especially true, where, as here, Petit suggests trying compounds (1a and 1b on page 915) which do not have the same substituents in the present invention and no suggestion of the same substituents of the present invention. Indeed, the only compound which

has four substituents on the phenanthrene structure.(compound 3 on page 915) is taught away by virtue of its CNS toxicity (Petit, p. 916 top paragraph). There is simply no way of combining Petit and Faber to produce the presently claimed compositions, especially given that Faber does not even mention biological activity of the compounds which are disclosed.

For the above reasons, Applicant respectfully asserts that the claims set forth in the amendment to the application of the present invention are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited. Applicants have neither cancelled nor added any claim. No fee is due for the presentation of this amendment.

An extension of time of two months and the appropriate fee is submitted herewith. If any additional fee is due or any overpayment has been made, please charge/credit Deposit Account No. 04-0838.

If the Examiner wishes to discuss the present application in order to advance prosecution, he is cordially requested to call the undersigned attorney at the telephone number indicated below.

Respectfully submitted,

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